

The Prevalence of Chronic Kidney Disease in Hypertensive Patients in Primary Care in Hong Kong: A Cross-Sectional Study

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Abstract

Background

To identify the prevalence of Chronic Kidney Disease (CKD) in Chinese hypertensive population managed in a local public primary care clinic and to explore its associated risk factors.

Methods

Medical records of Chinese adult hypertensive patients (> 18 years of age) who had been followed up in a public general outpatient clinic (GOPC) from 1 Jan 2018 to 30 Jun 2018 were retrieved and reviewed, and a sample group was randomly selected. Demographic, clinical parameters including age, gender, smoking status, body weight, height, systolic and diastolic blood pressure, biochemical data, and comorbidities were collected from the Computer Management System (CMS). Estimated glomerular filtration rate (eGFR) was calculated by using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. CKD was defined as eGFR < 60 ml/min/1.73m² and staged according to [Kidney Disease Improving Global Outcomes \(KDIGO\) 2012](#) criteria. Student's t-test was used to analyze continuous variables and the Chi-squared test was used for categorical data. Multivariate Logistic regression was used to examine the association between CKD and variable associated factors. All statistical tests were two-sided, and a P-value of <0.05 was considered significant.

Results

Among the 993 Chinese hypertensive patients included in the final analysis, 152 were found to have CKD, with overall prevalence being 15.3%. In addition, the prevalence of CKD increased with the ageing of the population. In multivariate analysis, associated factors for CKD included age (OR 4.3 for every 10 years increase), history of congestive heart failure (OR 7.2), diabetes mellitus (OR 1.8), gout (OR 3.2), number of anti-hypertensive medications (OR 1.6) and high-density lipoprotein cholesterol level (OR 0.38).

Conclusions

15.3% of Chinese adult hypertensive patients have CKD. Associated factors for CKD include older age, concomitant cardiovascular disease, diabetes mellitus, gout, and lipid disorder. Family physicians should make a concerted effort in early recognition of these risk factors for CKD among HT patients.

Introduction

Chronic kidney disease (CKD) is a worldwide public health problem.^[1] In [Kidney Disease Improving Global Outcome \(KDIGO\) 2012 clinical guideline](#),^[2] CKD is defined as abnormalities of kidney structure or function, present for more than 3 months, with implications for health. It is confirmed to be associated with an increased risk of cardiovascular comorbidities and mortality^[3, 4] as well as progression to end stage renal disease (ESRD) that is dialysis dependent.^[5, 6] In our daily practice, CKD refers to CKD stage 3

to 5 in the KDIGO CKD staging system, which is defined as estimated glomerular filtration rate (eGFR) being less than 60 ml/min/1.73 m². Extensive studies have shown that this group of patients carries a particularly high risk for complications and adverse outcomes. [7, 8]

The prevalence of CKD in the general population varies in regions, e.g. 8.7% in selected countries in Africa, 13.1% in Indian subcontinent, 14.7% in Australia, 15.5% in North America, 18.4% in Europe, 13.7% in Japan and South Korea, 13.2% in Greater China region, with considerable international variation.^[9] In Hong Kong, a screening study showed the prevalence of positive ($\geq 1+$) urine dipstick for protein, glucose, blood, protein or blood, any urine abnormality was 3.2%, 1.7%, 13.8%, 16%, 17.4%, respectively in apparently “healthy” (asymptomatic and without history of DM, HT, or CKD) individuals.^[10]

Hypertension (HT) is a well-recognized risk factor for CKD. According to the United States Renal Data System (USRDS) 2019 Annual Data Report ^[11], hypertension is the second leading cause of ESRD. As suggested by the Asian Forum for Chronic Kidney Disease Initiatives (AFCKDI)^[12], hypertensive patients are the target population for CKD screening. Various studies reported CKD prevalence in HT patients among 1.7–26.0% in different ethnic population in Europe, ^[13] the US,^[14] and Taiwan.^[15] A recent study in Hong Kong^[16] reported 22.0 per 1000 person-years for the incidence rate of CKD in local hypertensive patients. However, the study of CKD prevalence in HT patients in Hong Kong is still lacking despite the fact that many hypertensive patients followed-up in primary care have renal impairment.

Method

Aim

The objective of this study is to explore the prevalence of CKD in hypertensive patients in a public primary care clinic and to identify the possible associated factors.

Study design and setting

It is a cross-sectional study in a public primary care clinic.

Study population

Inclusion criteria

Chinese HT patients with International Classification of Primary Care (ICPC) code K86 (uncomplicated HT) or K87 (complicated HT) in the Clinical Management System (CMS), who had at least one follow up in a public primary care clinic from 01/01/2018 to 30/06/2018 and had at least two sets of serum renal function tests (RFT) done 3 months apart in the previous 3 years were included.

Exclusion criteria

1. non-Chinese HT patients

2. wrongly labeled HT
3. HT patients who had no blood test done in the previous 3 years.

Definition of CKD and staging

Calculation of eGFR

eGFR was calculated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation ^[17]:

$$\text{eGFR} = 141 \times \min(\text{SCr}/\kappa, 1)^\alpha \times \max(\text{SCr}/\kappa, 1)^{-1.209} \times 0.993^{\text{Age}} \times 1.018 \text{ [if female]} \times 1.159 \text{ [if Black]}; \kappa = 0.7 \text{ (females) or } 0.9 \text{ (males)}; \alpha = -0.329 \text{ (females) or } -0.411 \text{ (males)}; \min = \text{indicates the minimum of } \text{SCr}/\kappa \text{ or } 1; \max = \text{indicates the maximum of } \text{SCr}/\kappa \text{ or } 1; \text{ age} = \text{years}; \text{Scr in mg/dL}$$

Persistence of kidney abnormality

The latest two serum creatinine levels were retrieved from the CMS, which were at least 3 months apart. The mean eGFR was used for diagnosis and staging of CKD.

CKD definition and staging

CKD was defined as eGFR < 60 mL/min/1.73 m². According to Kidney Disease Improving Global Outcomes (KDIGO) 2012 criteria ^[2], patients with were further classified into the following stages:

CKD 3a: eGFR 45–59 ml/min/1.73 m²;

CKD 3b: eGFR 30–44 ml/min/1.73 m²;

CKD4: eGFR 15–29 ml/min/1.73 m²;

CKD5: eGFR < 15 ml/min/1.73 m².

All laboratory assays were performed in accredited laboratories by the College of American Pathologists, the Hong Kong Accreditation.

Determination of variables

Each recruited patients' age, gender, smoking status, body mass index (BMI), blood pressure, fasting sugar level and lipid profile were retrieved from the CMS. The patient was considered a smoker if he/she currently smoked or was within the first 6 months of quitting. The BMI was calculated as body weight (kg)/ body height² (m²). BMI > = 25 kg/m² was defined as obesity (Centre for Health Protection 2010 criteria). Systolic and diastolic blood pressure (SBP and DBP) were averaged for all the outpatient encounters from 01/01/2018 to 30/06/2018. The most recent blood tests for glucose and lipid profile were used for data analysis if more than one test had been performed during the study period.

Definition of comorbidities

The comorbidities were identified from both ICPC and International Classification of Diseases (ICD) -9 codes, as following:

Stroke / transient ischaemic attack (TIA): ICPC: K89, K90, K91; ICD-9: 430, 431, 432, 433, 434, 435, 436, 437, 438; ,

Ischaemic heart disease (IHD): ICPC: K74, K75, K76; ICD-9: 410, 411, 412, 413, 414 ;

Congestive heart failure (CHF): ICPC: K77; ICD-9: 428;

Atrial fibrillation (AF): ICPC: K78; ICD-9: 427.3;

Peripheral vascular disease (PVD); ICPC: K92; ICD-9: 443;

Diabetes mellitus (DM): ICPC: T89, T90; ICD-9: 250;

Gout: ICPC: T92; ICD-9: 274;

Chronic obstructive pulmonary disease (COPD): ICPC: R95; ICD-9: 491, 492, 494, 496.

Medications

Dispensary records were reviewed. The following medications were recorded: the current use of antihypertensive drugs, lipid-lowering agents, anti-platelet; urate-lowering agents; Non-steroid anti-inflammatory drugs (NSAIDs).

Sample size estimation

One proportion cross-sectional formula was used to calculate the sample size (website <http://www2.ccrb.cuhk.edu.hk/stat/epistud.htm>). Assume Probability of type 1 error is 0.01, prevalence proportion p is 0.15, estimated effect size is 1, desired level of absolute precision is 0.03, the required sample size is 940. To allow the room for sample exclusion (~ 20%), a total of 1200 patients was randomly selected by online (<https://www.randomizer.org/>) generated random numbers for data analysis.

Statistical analysis

Statistical calculations were completed using SPSS 19 (IBM SPSS Statistics version 19).

Continuous variables were described as mean and standard deviation, while qualitative variables were expressed as numbers and percentage. T-test was used to compare quantitative variables and the Chi-squared test for categorical variables. Mantel-Haenszel test was used for trend between age groups and CKD prevalence. Multivariate logistic regression analysis was used to identify the risk factors for the presence of CKD. All statistical tests were two-sided, and a P value of less than 0.05 was considered significant.

Results

Study population and sampling process

From 01/01/2018 to 30/06/2018, totally 17,689 HT patients had at least one follow-up visit in the clinic. Among them, 1200 patients were randomly selected, from which 207 cases were excluded, including 101 Non-Chinese, 2 wrongly labeled HT patients and 104 cases who had no repeated RFT tests 3 months apart. Therefore, the remaining 993 cases were included in the final analysis. The selection and sampling process was summarized in Fig. 1.

The demographics and comorbidities of HT patients were demonstrated in Table 1. Among the 993 patients included in data analysis, 489 were female and 504 were male, with an average age of 68.9 ± 10.9 years. 73 (7.4%) were current smokers and 166 (16.6%) were ex-smokers. With regards to comorbidities, 438 (44.1%) had DM, 100 (10.1%) had stroke / TIA, 54 (5.4%) had IHD, 25 (2.5%) had AF, 12 (1.2%) had CHF, 69 (6.9%) had gout, 21 (2.1%) had COPD, and 3 (0.3%) had PVD.

Table 1
Demographics and comorbidities of HT patients included in data analysis

	Total (n = 993)
Age (year)	68.9 ± 10.9
Gender	489 (49.2%)
Female n(%)	504(50.8%)
Male n(%)	
BMI (kg/m ²)	25.7 ± 4.1
Obesity n (%)	514(51.8%)
Smoking status n(%)	
Smoker	73(7.4%)
Ex-smoker	165(16.6%)
Non-smoker	755(76.0%)
Comorbidities n (%)	
cardiovascular disease	
Stroke / TIA	100(10.1%)
IHD	54(5.4%)
CHF	12(1.2%)
AF	25(2.5%)
PVD	3(0.3%)
Metabolic disorder	
Diabetes	438(44.1%)
Gout	69(6.9%)
COPD	21(2.1%)
Data are shown as mean ± standard deviation or No. (%) of cases	
TIA, transient ischaemic attack; IHD, ischaemic heart disease; CHF, congestive heart failure; AF, atrial fibrillation; PVD, peripheral vascular disease; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease.	

Prevalence of CKD and distribution in age groups

As shown in Table 2, as defined by eGFR < 60 ml/min/1.73 m², the prevalence of CKD was 17.5% in male, 13.1% in female, and **15.3% overall**. Male patients seemed to have a higher prevalence of CKD than female, but the difference was not significant (p = 0.065). The prevalence of CKD stage 3a, 3b, 4 and 5 in hypertensive patients were 10.1%, 4.4%, 0.6% and 0.2% respectively.

Table 2
CKD prevalence among HT patients in the primary care setting

	Male (n = 504)		Female (n = 489)		Total (n = 993)	
Creatinine (umol/L)	92.4 ± 25.2		68.8 ± 19.9		80.9 ± 25.6	
eGFR (mL/min/1.73 m ²)	76.0 ± 18.2		80.4 ± 17.5		78.2 ± 18.0	
	N	%	N	%	N	%
Non-CKD (eGFR ≥ 60)	416	82.5	425	86.9	841	84.7
CKD (eGFR < 60)	88	17.5	64	13.1	152	15.3
CKD3a (45–59)	55	10.9	45	9.2	100	10.1
CKD3b (30–44)	29	5.8	15	3.1	44	4.4
CKD4 (15–29)	3	0.6	3	0.6	6	0.6
CKD5 (< 15)	1	0.2	1	0.2	2	0.2
Data are shown as mean ± standard deviation						
eGFR: estimated glomerular filtration rate; p = 0.065 for comparison of CKD prevalence between male and female patients						

The prevalence of CKD in various age groups were 0% in 30–39 and 40–49 age groups, 2.4% in 50–59 age group, 5.0% in 60–69 age group, 18.4% in 70–79 age group, 41.5% in 80–89 age group, and 70.8% in 90 or above age group. Figure 2 showed an apparent positive relationship between the prevalence of CKD and age groups, the elder the age group, the higher the prevalence of CKD (trend p < 0.001).

Factors associated with CKD

Table 3 summarized the univariate analysis of risk factors associated with CKD among HT patients. It showed that HT patients with CKD were older (79.7 ± 8.7 vs 67.0 ± 10.1 years, p < 0.001), had higher SBP (129.6 ± 10.9 vs 127.4 ± 8.8 mmHg, p 0.008) but lower DBP (67.7 ± 8.9 vs 73.2 ± 8.5 mmHg, p < 0.001) than non-CKD group. Their comorbidity rate was also higher with stroke / TIA (17.8% vs 8.7%, p 0.002), CHF (5.9% vs 0.4%, p < 0.001), AF (5.3% vs 2.0%, p 0.042), DM (63.2% vs 40.7%, p < 0.001) and gout (15.8% vs 5.4%, p < 0.001). Patients with CKD were found to have lower concentration of total cholesterol (4.1 ± 0.7 vs 4.5 ± 0.8 mmol/L, p < 0.001), LDL (2.1 ± 0.6 vs 2.4 ± 0.7 mmol/L, p < 0.001), HDL level (1.3 ± 0.4 vs 1.4 ± 0.4 mmol/L, p 0.002). They were on more numbers of anti-hypertensive medications (2.2 ± 1.0 vs 1.7 ± 0.8, p < 0.001), including ACEI/ARB (61.2% vs 49.0%, p 0.006), alpha-blocker (32.9% vs 12.4%, p <

0.001), statin (70.4% vs 58.7%, p 0.007), anti-platelet (30.9% vs 15.2%, p < 0.001) and urate-lowering drug use (9.2% vs 2.5%, p < 0.001).

Further analysis using the Logistic regression to assess the contribution of multiple variables, as shown in Table 4, significantly associated factors for CKD were older age (OR 4.26 for every 10 years increase, p < 0.001), history of CHF (OR 7.23, p 0.024), DM (OR 1.80, p 0.009), gout (OR 3.18, p 0.001), lower level of HDL (OR 0.38, p 0.002) and more numbers of anti-HT medications (OR 1.58, p < 0.001).

Table 3
Univariate analysis of associated factors for CKD among HT cases

	Non CKD (eGFR ≥ 60) (n = 841)	CKD (eGFR < 60) (n = 152)	P value
Age (years)	67.0 ± 10.1	79.7 ± 8.7	< 0.001
Gender (Female%)	425(50.5%)	64(42.1%)	0.064
BMI (kg/m ²) *	25.7 ± 4.0	25.8 ± 4.2	0.901
Obesity(BMI ≥ 25)%	257/506(50.8%)	56/98(57.1%)	0.270
Smoking status n(%)			0.263
Smoker	65(7.7%)	8(5.3%)	
Ex-smoker	134(15.8%)	31(20.4%)	
Non-smoker	642(76.3%)	113(74.3%)	
BP			
SBP(mmHg)	127.4 ± 8.8	129.6 ± 10.9	0.008
DBP(mmHg)	73.2 ± 8.5	67.7 ± 8.9	< 0.001
Cardiovascular disease n(%)			
Stroke / TIA	73(8.7%)	27(17.8%)	0.002
IHD	45(5.4%)	9(5.9%)	0.701
CHF	3(0.4%)	9(5.9%)	< 0.001
AF	17(2.0%)	8(5.3%)	0.042
PVD	1(0.1%)	2(1.3%)	0.063
Metabolic disorder n(%)			
Diabetes	342(40.7%)	96(63.2%)	< 0.001
Gout	45(5.4%)	24(15.8%)	< 0.001
COPD n(%)	17(2.0%)	4(2.6%)	0.548
BMI, body mass index; SBP, systolic BP; DBP, diastolic BP; TIA, transient ischaemic attack; IHD, ischaemic heart disease; CHF, congestive heart failure; AF, atrial fibrillation; PVD, peripheral vascular disease; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; TG, triglyceride; TC, total cholesterol; LDL, low density lipoprotein; HDL, high density lipoprotein; ACEI/ ARB, ACEI angiotensin converting enzyme inhibitor/angiotensin receptor blocker.			
*All data were complete, except for BMI (604 or 60.8% available in all 993 participants).			

	Non CKD (eGFR ≥ 60) (n = 841)	CKD (eGFR < 60) (n = 152)	P value
Fasting Glucose (mmol/L)	6.1 ± 1.4	6.3 ± 1.3	0.085
Lipid			
TG (mmol/L)	1.5 ± 0.9	1.4 ± 0.8	0.881
TC (mmol/L)	4.5 ± 0.8	4.1 ± 0.7	< 0.001
LDL (mmol/L)	2.4 ± 0.7	2.1 ± 0.6	< 0.001
HDL (mmol/L)	1.4 ± 0.4	1.3 ± 0.4	0.002
Medication use			
Anti-Hypertensive			
Number of medications	1.7 ± 0.8	2.2 ± 1.0	< 0.001
ACEI/ARB	412(49.0%)	93(61.2%)	0.006
CCB	652(77.5%)	121(79.6%)	0.598
Diuretics	42(5.0%)	12(7.9%)	0.171
Beta-blocker	232(27.6%)	53(34.9%)	0.053
Alpha-blocker	104(12.4%)	50(32.9%)	< 0.001
Statin	494(58.7%)	107(70.4%)	0.007
Anti-platelet	128(15.2%)	47(30.9%)	< 0.001
Urate-lowering drugs	21(2.5%)	14(9.2%)	< 0.001
<p>BMI, body mass index; SBP, systolic BP; DBP, diastolic BP; TIA, transient ischaemic attack; IHD, ischaemic heart disease; CHF, congestive heart failure; AF, atrial fibrillation; PVD, peripheral vascular disease; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; TG, triglyceride; TC, total cholesterol; LDL, low density lipoprotein; HDL, high density lipoprotein; ACEI/ ARB, ACEI angiotensin converting enzyme inhibitor/angiotensin receptor blocker.</p>			
*All data were complete, except for BMI (604 or 60.8% available in all 993 participants).			

Table 4
Multivariate Logistic regression analysis of associated factors for CKD among HT patients

Covariates	OR	95% C.I.		P-value
		Lower limit	Upper limit	
Age(every 10 yrs increase)	4.26	3.299	5.495	< 0.001
CHF	7.23	1.304	40.115	0.024
DM	1.80	1.155	2.797	0.009
Gout	3.18	1.604	6.317	0.001
HDL level	0.38	0.207	0.690	0.002
Number of HT medications	1.58	1.250	1.998	< 0.001

CHF, congestive heart failure; AF, atrial fibrillation; DM, diabetes mellitus; HDL, high density lipoprotein; OR, odds ratio. Only significant factors were listed (p-value < 0.05)

Discussion

Renal function test is essential to the diagnosis and staging of CKD. However, serum creatinine alone is not reliable to assess the renal function, as the serum creatinine concentration is influenced by GFR and other “non-GFR determinants” including the muscle bulk, dietary intake, renal tubular secretion and extrarenal creatinine elimination by the gastrointestinal tract.^[18]

Creatinine based eGFR estimation has evolved from Cockcroft-Gault (CG) formula^[19], Modification of Diet in Renal Disease (MDRD)^[20], to CKD-EPI equation^[17]. The CG formula is now mostly used to determine dosing adjustments for medications. MDRD equation has been widely used since its development in 1999 but may not be accurate at higher GFR levels, especially when eGFR is over 60 ml/min/1.73 m². In view of this, the National Kidney Disease Education Program (NKDEP) recommends against the reporting as a numeric value if eGFR is ≥ 60 ml/min/1.73 m² calculated by the MDRD equation.^[21] The CKD-EPI equation was developed in 2009 and it has less bias than the MDRD equation, especially when GFR is ≥ 60 ml/min/1.73 m², which enables the reporting of numeric values across all ranges of GFR. KDIGO 2012 guideline recommended the use of the CKD-EPI equation for evaluation of eGFR in adults.^[2] Hospital Authority in Hong Kong has completely turned to the CKD-EPI equation from the MDRD equation to report eGFR values in 2017. In this study, we used the CKD-EPI equation to calculate the eGFR and to stage CKD and this is consistent with the recommendations of the latest international guidelines.

Defined by eGFR < 60ml/min/1.73m², the prevalence of CKD varies though the world. In Europe, it varies between 1.7 to 11.5% in the general population, and 2.2-14.3% in hypertensive patients.^[13] In the United States, USRDS reported the CKD prevalence of 6.9% in the general population and 16.1% in the hypertensive population among participants of the National Health and Nutrition Examination Survey

(NHANES) 2013-2016 ^[14]. In Taiwan, a local cohort based study found 9.1% CKD prevalence in the general population and 26.0% in hypertensive individuals.^[15] Although all these literature provided prevalence of CKD defined by $eGFR < 60\text{ml/min}/1.73\text{m}^2$, there were heterogeneity in patient source and sampling (electoral rolls, general practitioners lists, cohort, etc.), age ranges (all ages or elderly), eGFR calculation methods (CG, MDRD, CKD-EPI equations), and definition of CKD (by eGFR calculation or by diagnostic codes). In our study, we found that CKD was present among 15.3% Chinese hypertensive patients, that was similar with those reported in the US and some European countries, but higher than other European countries and lower than Taiwan. The discrepancy could be due to the true difference or method diversity.

Although univariate analysis showed more risk factors could be related to CKD, the multivariate analysis after adjustment showed that significant factors associated with CKD were older age (OR 4.26 for every 10 years increase, $p < 0.001$), history of CHF (OR 7.23, $p = 0.024$), DM (OR 1.80, $p = 0.009$), gout (OR 3.18, $p = 0.001$), lower HDL (OR 0.38, $p = 0.002$), and more numbers of anti-HT medications (OR 1.58, $p < 0.001$).

Firstly, our study showed a strong positive correlation between older age and increased risk of CKD, which is consistent with previous studies both in the general population ^[22] and in hypertensive patients.^[23-25] There is a debate whether decreased GFR in older people represents an actual disease or a “normal ageing” phenomenon, as GFR declines steadily with ageing, beginning at age 30–40 years, with an apparent acceleration in the rate of decline after age 65–70 years.^[26] The subdivision of CKD stage 3 ($eGFR 30\text{-}59\text{ ml/min}/1.73\text{ m}^2$) into 3a ($eGFR 45\text{-}59\text{ ml/min}/1.73\text{ m}^2$) and 3b ($30\text{-}44\text{ ml/min}/1.73\text{ m}^2$), partially reflected the concept of the latter being more “pathologic” beyond natural aging with more complications. Furthermore, glomerular sclerosis, tubular atrophy and vascular sclerosis are associated with ageing.^[27] Given the fact that there appears to be increased risk of complications associated with decreased eGFR in older people irrespective of cause, KDIGO considers all individuals with persistently decreased GFR less than $60\text{ ml/min}/1.73\text{m}^2$ to have CKD, which is still the current standard of practice and research.

History of CHF was found to be a strong associated factor for CKD, as supported by other studies.^[28, 29] Actually sometimes they are considered concurrent chronic disease epidemics.^[30] CHF as the primary syndrome can experience secondary CKD, and vice versa, or both can coexist on the basis of shared risk factors. In this cross-sectional study, it is hard to tell which disease is primary and which is secondary.

It was not unexpected that DM was an associated factor with CKD, as DM itself is the leading cause of CKD and ESRD in developed countries. As a well-recognized microvascular complication, kidney impairment develops in approximately 30% of Type 1 DM patients and 40% Type 2 DM patients.^[30] Among the risk factors for Diabetic kidney disease initiation and progression, hyperglycemia and hypertension are the two most prominent factors.^[31]

An association between gout and CKD has been recognized for many years.^[32-34] The association could be bidirectional, with CKD as an independent risk factor for gout^[35] and gout patients potentially predisposing to CKD possibly by hyperuricemia, chronic inflammation or NSAIDs drug therapy.

Dyslipidemia is common but not universal in CKD patients. The presence of dyslipidaemia was affected by eGFR, presence of DM, the severity of proteinuria and nutrition.^[36] While KDIGO Work Group no longer recommended LDL-Cholesterol as the single indication/target for pharmacological therapy, some studies supported the role of low HDL-cholesterol in the development and progression of CKD.^[37, 38] However, the protective role of HDL in CKD is being challenged and needs further evidence.^[39]

Family physicians should enhance their awareness of the high prevalence of CKD among HT patients and pay particular attention to the presence of the above risk factors. A concerted effort should be made in early recognition and controlling of these risk factors and to prevent the development of CKD among HT patients.

Strength and limitations of the study

To the best of our knowledge, this is the first study to describe the CKD prevalence among HT cases managed in the primary care setting in Hong Kong. The patient source pool was relatively large (> 10000), and several associated factors were identified. All clinical and laboratory parameters of the data were retrieved from the computerized clinical management system (CMS) of the Hospital Authority, therefore recall bias was minimized. In renal function evaluation, we used 2 samples of serum creatinine with 3 months apart to confirm the persistence of impaired renal function, while most of the other studies use 1 sample only for simplicity. We also used the latest CKD-EPI equation to calculate eGFR and classify CKD, according to KDIGO's recommendation, more reliable with less bias compared with the MDRD equation, and consistent with the latest international studies. In collecting comorbidities information, we used both ICPC and ICD coding, to avoid missing the diagnosis information provided by hospital care and specialist outpatient clinic record. Our data showed significant better completeness of diagnosis information in this combination coding system method, compared with ICPC code alone.

However, there were several limitations to this study. Firstly, the complete CKD information should address the evidence of renal damage besides renal function, typically proteinuria or albuminuria. However, not all HT patients universally checked urine protein/albumin. The practical definition of CKD as eGFR < 60ml/min/1.73m² simplified the process and the validity was supported by international^[21] and local studies^[16]. The prevalence reported by this study was compared with the data with the same CKD definition. Secondly, this was a single centre data from a public primary care clinic, therefore selection bias existed. Larger scale study could overcome this limitation. Patients with more advanced CKD stages would be referred to secondary care, thus the percentage of CKD 4/5 patients could be underestimated. The results may not be applicable to the private sector or secondary care setting. Lastly, given the cross-sectional design of the study, it could not establish a causal relationship between associated factors and

CKD development. Prospective cohort study or interventional study would help provide more information on this regard.

Conclusion

In Chinese hypertensive patients followed-up in a primary care clinic, the prevalence of chronic kidney disease with eGFR being less than 60ml/min/1.73m² was **15.3%** by CKD-EPI equation. The prevalence showed an apparently increasing trend in elderly age groups. The associated factors for CKD were older age (OR 4.3 for every 10 years increase), history of CHF (OR 7.2), DM (OR 1.8), gout (OR 3.2), number of anti-HT medications (OR 1.6) and low HDL level (OR 0.38). The family physician should make a concerted effort in early recognition and controlling of these risk factors.

Abbreviations

ACEI, Angiotensin-converting enzyme inhibitor

AF, Atrial fibrillation

AFCKDI, Asian Forum for Chronic Kidney Disease Initiatives

ARB, Angiotensin receptor blocker

BMI, Body mass index

CG, Cockcroft-Gault formula

CHF, Congestive heart failure

CKD, Chronic Kidney Disease

CMS, Computer Management System

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration equation

COPD, Chronic obstructive pulmonary disease

DBP, Diastolic blood pressure

DM, Diabetes mellitus

eGFR, Estimated glomerular filtration rate

ESRD, End stage renal disease

GOPC, General outpatient clinic

HDL, high density lipoprotein

HT, Hypertension

ICD -9, International Classification of Diseases -9

ICPC, International Classification of Primary Care

IHD, Ischaemic heart disease

KDIGO, Kidney Disease Improving Global Outcomes

LDL, low density lipoprotein

MDRD, Modification of Diet in Renal Disease

NHANES, National Health and Nutrition Examination Survey

NKDEP, National Kidney Disease Education Program

NSAIDs, Non-steroid anti-inflammatory drugs

OR, odds ratio

PVD, Peripheral vascular disease

RFT, Renal function test

SBP, Systolic blood pressure

SPSS, Statistical Product and Service Solutions

TIA, Transient ischaemic attack

USRDS, United States Renal Data System

Declarations

Ethical approval

The study was approved by the Cluster Research Ethics Committee. Ref: KC/KE-18-0196/ER-1. This is an observational study collecting existing data via Clinical Management System Retrieving Software without sensitive or identifiable personal information (name or ID), without affecting patient's management, and reported in aggregate level. So exemption of consent was applied and approved by the Institutional Review Board (IRB) or Research Ethics Committee (REC) of Hospital Authority in Hong Kong.

Consent for publication

Not applicable

Availability of data

The data was stored and retrievable in the computer system of Hospital Authority Hong Kong, with restricted access according to “need to care” policy, therefore not accessible to the public. Researchers are allowed to retrieve and analyze data under approval from Ethical committee.

Competing interests

The authors declare that they have no competing interest.

Funding

No funding.

Author's contributions

Xu collected, analyzed and interpreted the patient data. Li supervised the overall research, clinical work and patient care. Chen gave comments and major revisions on the design of the research and writing the manuscript. All authors read and approved the final manuscript.

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References

- [1] Inker LA, Coresh J, Levey AS, Tonelli M, Muntner P. Estimated GFR, albuminuria, and complications of chronic kidney disease. *J Am Soc Nephrol.* 2011. 22(12): 2322-31.
- [2] Stevens PE, Levin A, Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group Members. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. *Ann Intern Med.* 2013. 158(11): 825-30.
- [3] Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med.* 2004. 351(13): 1296-305.
- [4] Chronic Kidney Disease Prognosis Consortium, Matsushita K, van der Velde M, et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in

general population cohorts: a collaborative meta-analysis. *Lancet*. 2010. 375(9731): 2073-81.

[5] Gansevoort RT, Matsushita K, van der Velde M, et al. Lower estimated GFR and higher albuminuria are associated with adverse kidney outcomes. A collaborative meta-analysis of general and high-risk population cohorts. *Kidney Int*. 2011. 80(1): 93-104.

[6] Mahmoodi BK, Matsushita K, Woodward M, et al. Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without hypertension: a meta-analysis. *Lancet*. 2012. 380(9854): 1649-61.

[7] Hsu CY, Ordoñez JD, Chertow GM, Fan D, McCulloch CE, Go AS. The risk of acute renal failure in patients with chronic kidney disease. *Kidney Int*. 2008. 74(1): 101-7.

[8] Astor BC, Matsushita K, Gansevoort RT, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with mortality and end-stage renal disease. A collaborative meta-analysis of kidney disease population cohorts. *Kidney Int*. 2011. 79(12): 1331-40.

[9] Hill NR, Fatoba ST, Oke JL, et al. Global Prevalence of Chronic Kidney Disease - A Systematic Review and Meta-Analysis. *PLoS One*. 2016. 11(7): e0158765.

[10] Li PK, Kwan BC, Leung CB, et al. Prevalence of silent kidney disease in Hong Kong: the screening for Hong Kong Asymptomatic Renal Population and Evaluation (SHARE) program. *Kidney Int Suppl*. 2005. (94): S36-40.

[11] System USRD. US Renal Data System 2019 Annual Data Report: Epidemiology of Kidney Disease in the United States. https://www.usrds.org/2019/download/USRDS_2019_ES_final.pdf. : 31-2.

[12] Li PK, Chow KM, Matsuo S, et al. Asian chronic kidney disease best practice recommendations: positional statements for early detection of chronic kidney disease from Asian Forum for Chronic Kidney Disease Initiatives (AFCKDI). *Nephrology (Carlton)*. 2011. 16(7): 633-41.

[13] Brück K, Stel VS, Gambaro G, et al. CKD Prevalence Varies across the European General Population. *J Am Soc Nephrol*. 2016. 27(7): 2135-47.

[14] [Accessed 30 Oct 2019]System USRD. US Renal Data System 2018 Annual Data Report. Chapter 1: CKD in the General Population. https://www.usrds.org/2018/download/v1_c01_GenPop_18_usrds.pdf .

[15] Tsai MH, Hsu CY, Lin MY, et al. Incidence, Prevalence, and Duration of Chronic Kidney Disease in Taiwan: Results from a Community-Based Screening Program of 106,094 Individuals. *Nephron*. 2018. 140(3): 175-184.

[16] Wan E, Yu E, Chin WY, Fong D, Choi E, Lam C. Association of Blood Pressure and Risk of Cardiovascular and Chronic Kidney Disease in Hong Kong Hypertensive Patients. *Hypertension*. 2019. 74(2): 331-340.

- [17] Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med.* 2009. 150(9): 604-12.
- [18] Stevens LA, Levey AS. Measured GFR as a confirmatory test for estimated GFR. *J Am Soc Nephrol.* 2009. 20(11): 2305-13.
- [19] Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron.* 1976. 16(1): 31-41.
- [20] Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med.* 1999. 130(6): 461-70.
- [21] Myers GL, Miller WG, Coresh J, et al. Recommendations for improving serum creatinine measurement: a report from the Laboratory Working Group of the National Kidney Disease Education Program. *Clin Chem.* 2006. 52(1): 5-18.
- [22] Zhang QL, Rothenbacher D. Prevalence of chronic kidney disease in population-based studies: systematic review. *BMC Public Health.* 2008. 8: 117.
- [23] Rahman M, Brown CD, Coresh J, et al. The prevalence of reduced glomerular filtration rate in older hypertensive patients and its association with cardiovascular disease: a report from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. *Arch Intern Med.* 2004. 164(9): 969-76.
- [24] Ravera M, Noberasco G, Weiss U, et al. CKD awareness and blood pressure control in the primary care hypertensive population. *Am J Kidney Dis.* 2011. 57(1): 71-7.
- [25] Leoncini G, Viazzi F, Rosei EA, et al. Chronic kidney disease in hypertension under specialist care: the I-DEMAND study. *J Hypertens.* 2010. 28(1): 156-62.
- [26] Glassock RJ, Winearls C. Ageing and the glomerular filtration rate: truths and consequences. *Trans Am Clin Climatol Assoc.* 2009. 120: 419-28.
- [27] Sobamowo H, Prabhakar SS. The Kidney in Aging: Physiological Changes and Pathological Implications. *Prog Mol Biol Transl Sci.* 2017. 146: 303-340.
- [28] Kottgen A, Russell SD, Loehr LR, et al. Reduced kidney function as a risk factor for incident heart failure: the atherosclerosis risk in communities (ARIC) study. *J Am Soc Nephrol.* 2007. 18(4): 1307-15.
- [29] Bagshaw SM, Cruz DN, Aspromonte N, et al. Epidemiology of cardio-renal syndromes: workgroup statements from the 7th ADQI Consensus Conference. *Nephrol Dial Transplant.* 2010. 25(5): 1406-16.
- [30] McCullough PA, Philbin EF, Spertus JA, et al. Confirmation of a heart failure epidemic: findings from the Resource Utilization Among Congestive Heart Failure (REACH) study. *J Am Coll Cardiol.* 2002. 39(1):

[31] Alicic RZ, Rooney MT, Tuttle KR. Diabetic Kidney Disease: Challenges, Progress, and Possibilities. *Clin J Am Soc Nephrol*. 2017. 12(12): 2032-2045.

[32] Fessel WJ. Renal outcomes of gout and hyperuricemia. *Am J Med*. 1979. 67(1): 74-82.

[33] Stack AG, Johnson ME, Blak B, et al. Gout and the risk of advanced chronic kidney disease in the UK health system: a national cohort study. *BMJ Open*. 2019. 9(8): e031550.

[34] Roughley M, Sultan AA, Clarson L, et al. Risk of chronic kidney disease in patients with gout and the impact of urate lowering therapy: a population-based cohort study. *Arthritis Res Ther*. 2018. 20(1): 243.

[35] Wang W, Bhole VM, Krishnan E. Chronic kidney disease as a risk factor for incident gout among men and women: retrospective cohort study using data from the Framingham Heart Study. *BMJ Open*. 2015. 5(4): e006843.

[36] Kasiske BL. Hyperlipidemia in patients with chronic renal disease. *Am J Kidney Dis*. 1998. 32(5 Suppl 3): S142-56.

[37] Zoppini G, Targher G, Chonchol M, Perrone F, Lippi G, Muggeo M. Higher HDL cholesterol levels are associated with a lower incidence of chronic kidney disease in patients with type 2 diabetes. *Nutr Metab Cardiovasc Dis*. 2009. 19(8): 580-6.

[38] Kawachi K, Kataoka H, Manabe S, Mochizuki T, Nitta K. Low HDL cholesterol as a predictor of chronic kidney disease progression: a cross-classification approach and matched cohort analysis. *Heart Vessels*. 2019. 34(9): 1440-1455.

[39] Kronenberg F. HDL in CKD-The Devil Is in the Detail. *J Am Soc Nephrol*. 2018. 29(5): 1356-1371.

Figures

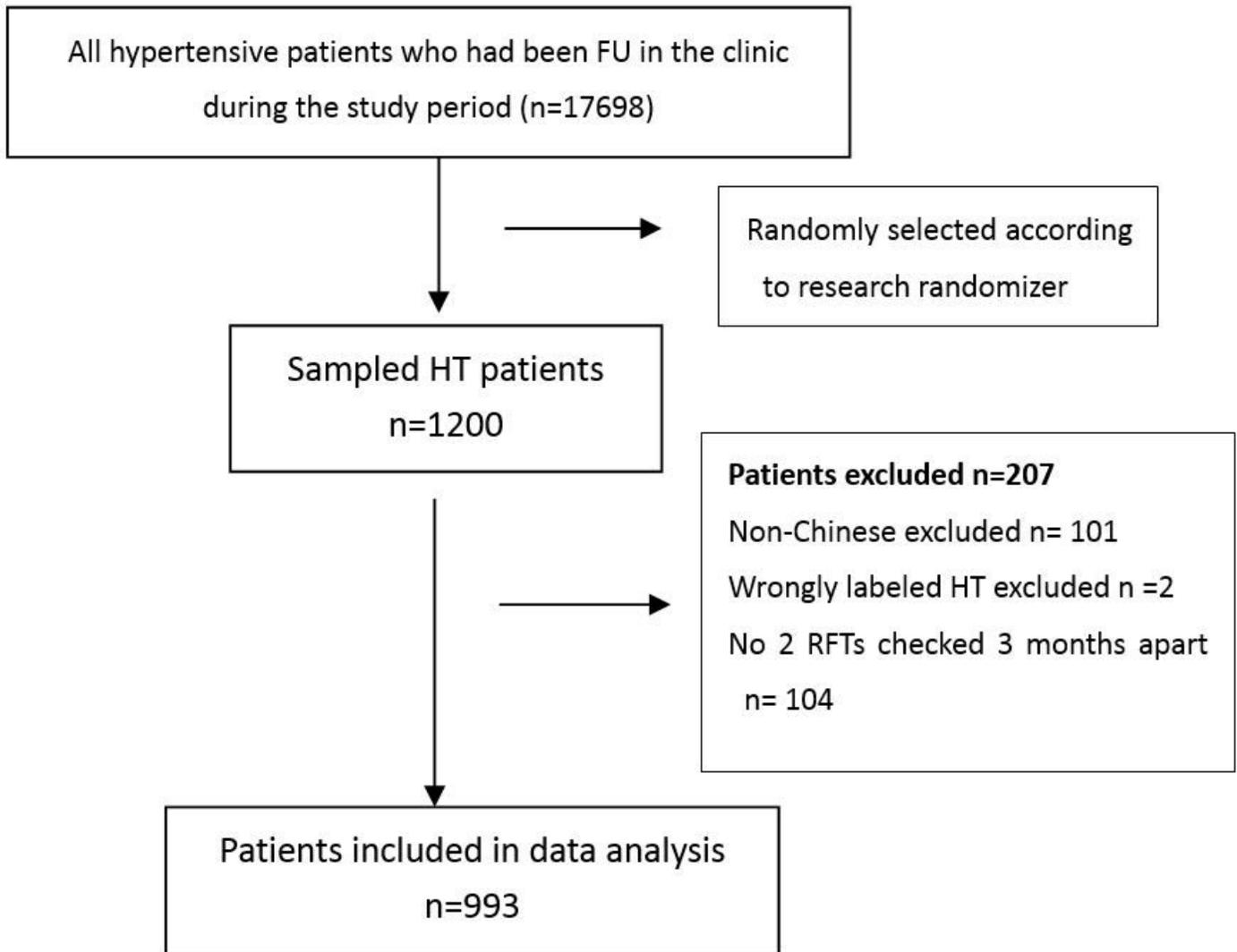


Figure 1

Flow chart of case selection who fulfilled the inclusion criteria for the study.

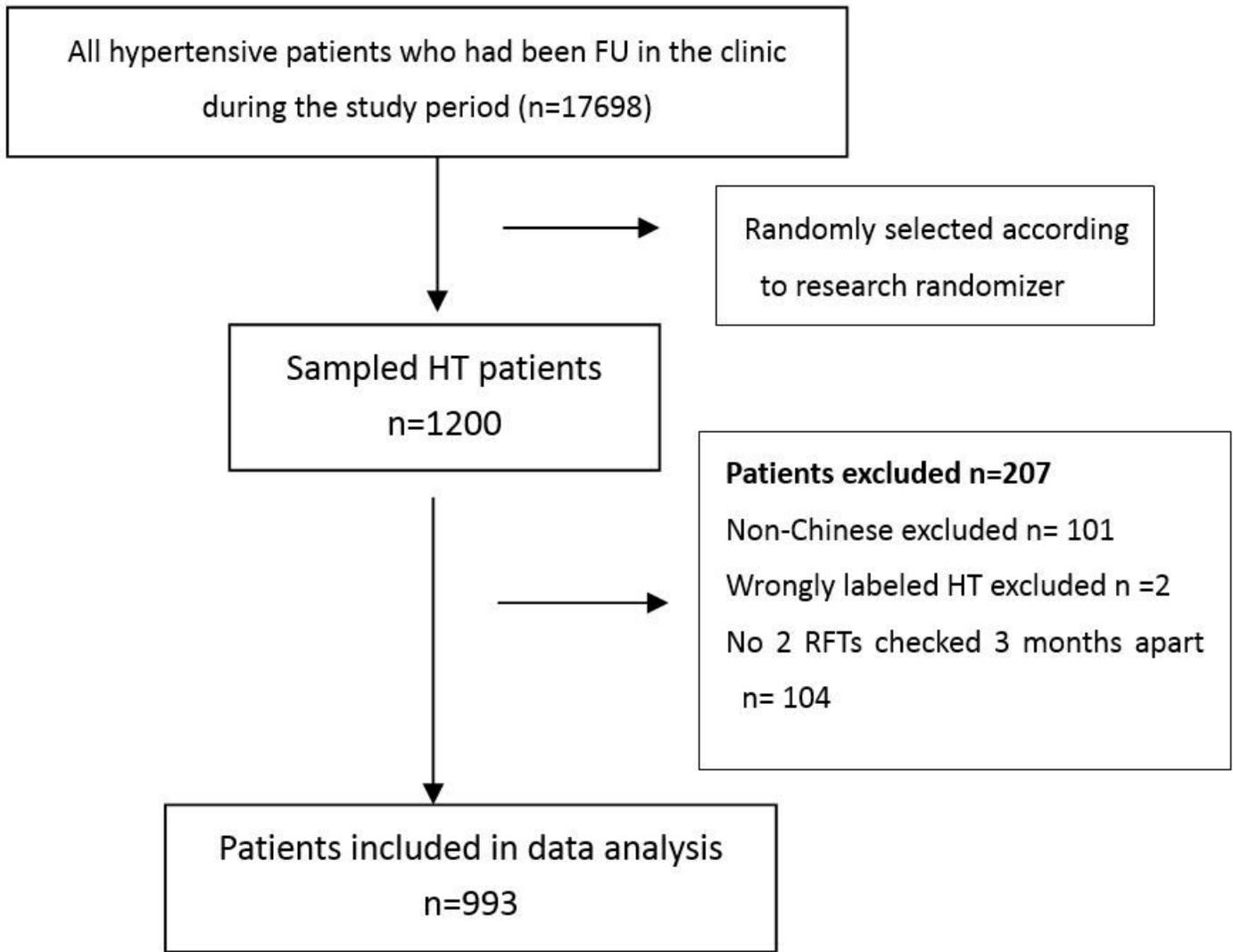


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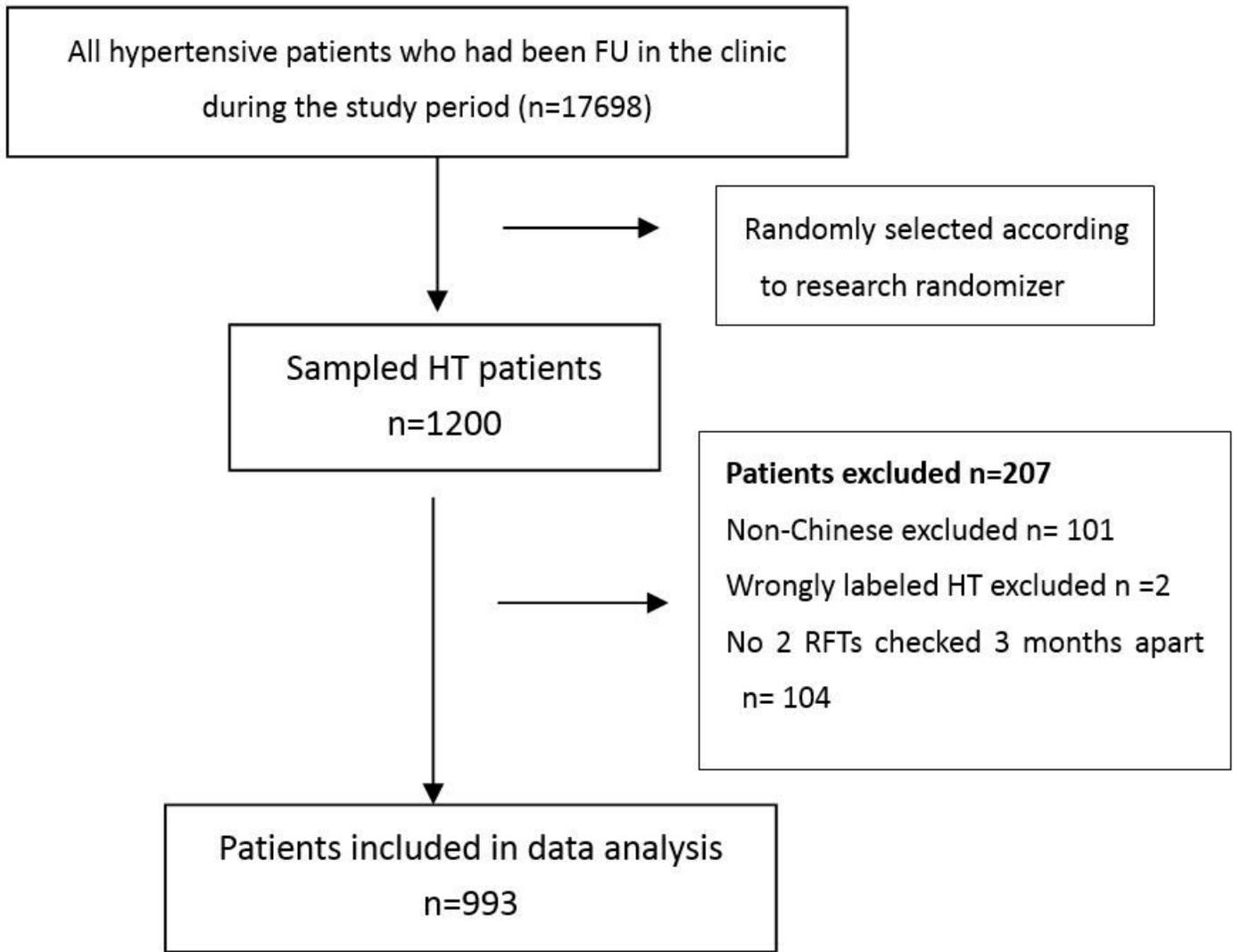


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Flow chart of case selection who fulfilled the inclusion criteria for the study.

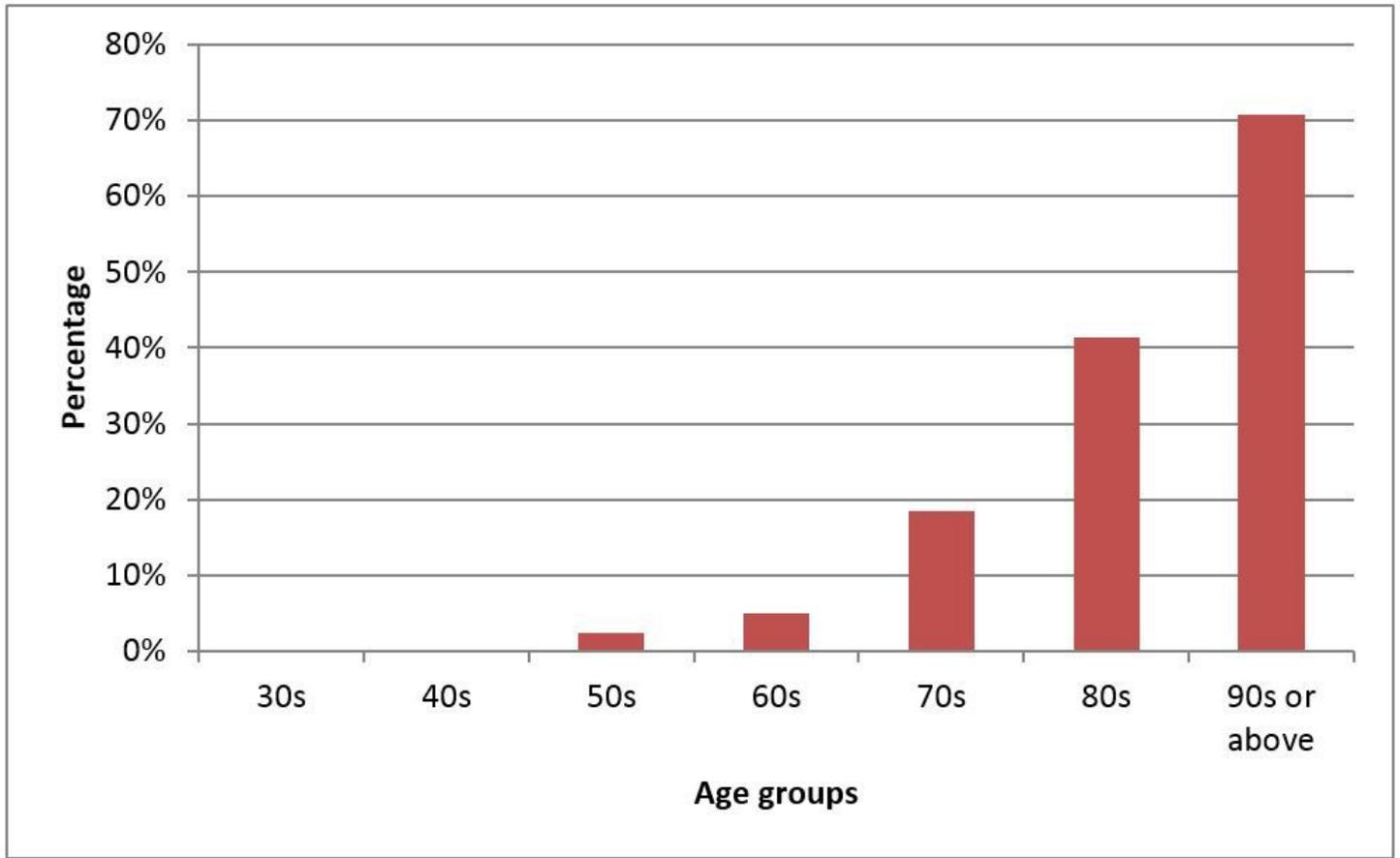


Figure 2

Prevalence of CKD by age groups of HT patients (Trend $P < 0.001$)

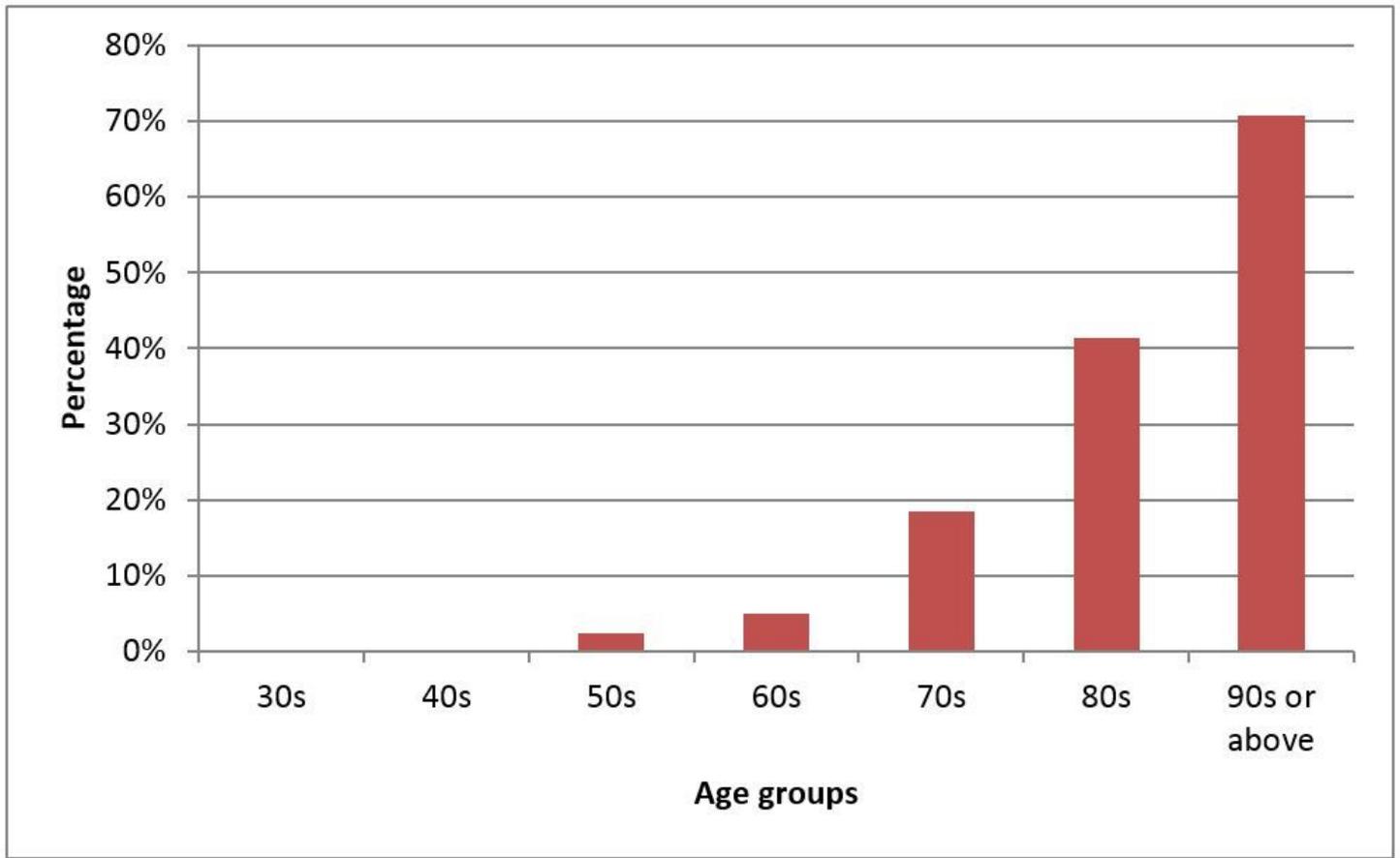


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Prevalence of CKD by age groups of HT patients (Trend $P < 0.001$)

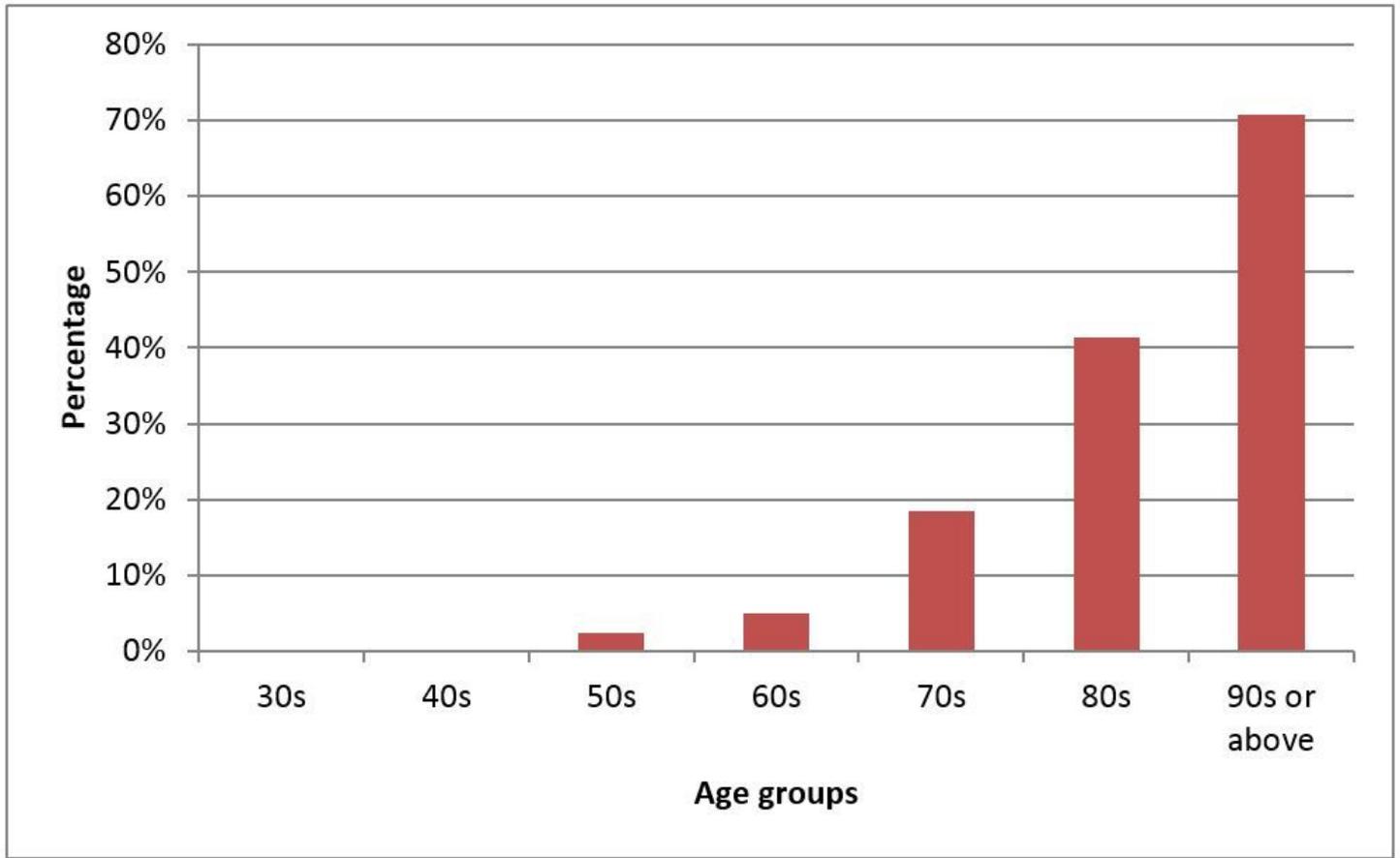


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